UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,776	03/29/2004	David F. Muir	UF-336XC3D1	4996

51414 7590 02/07/2006

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
EXCHANGE PLACE
BOSTON, MA 02109-2881

EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/812,776	MUIR, DAVID F.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-23,30-40,42-123* is/are pending in the application.

4a) Of the above claim(s) *57-115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-23,30-40,42-56 and 116-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the Group I (original claims 1-56, drawn to a method for preparing a nerve tissue graft by culturing the nerve tissue) in the reply filed on 11/23/2005 is acknowledged. The traversal is on the ground(s) that there is no serious burden in searching and examining all groups of claims. This is not found persuasive because different groups of claims are drawn to products and methods having different scope as claimed and, thus, the references that would be applied to one group of claims would not necessarily anticipate or render obvious the other group(s). Moreover, as to the question of burden of search, classification of subject matter is also an indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exists. Clearly different searches and issues are involved with each group. For these reasons, the restriction requirement is deemed proper and is adhered to. The restriction requirement is hereby made FINAL.

Claims 57-115 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups of inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/23/2005.

Claims 1-4, 6-23, 30-40, 42-56 as amended (11/23/2005) and new claims 116-123 (11/23/2005) are under examination in the instant office action.

Claims 5, 24-29 and 41 are canceled by applicant.

Claim Rejections - 35 USC § 112

Claims 1-4, 6-23, 30-40, 42-56 and 116-123 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 38 and 16 are indefinite because the meaning of term "nerve tissue" is uncertain. Biological tissue is made up of cells and, thus, the difference between claimed "nerve tissue'" and plurality of nervous cells is uncertain. Claims are indefinite with regard to the claimed term "predegenerating" conditions in the lack of specific definitions.

Claims 1, 6, 38, 116 are indefinite and incomplete because it is not particularly clear what steps are active steps in the method for preparing nerve tissue as intended. For example: phrase "subsequently implanted" is not considered to be an active step.

Claims 2-4 are indefinite and incomplete because the it is unclear whether the claimed limitations drawn to assays are active steps that are required by the claimed method or the claimed limitations are intended effects (inherent characteristics) of final nerve tissue in the method for preparing nerve tissue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-4, 6-15, 17-21, 30-51, 53-56, 116-123 are rejected under 35 U.S.C. 102(b) as being anticipated by La Fleur et al. (IDS reference; J. Exp. Med. 1996, 184:2311-2326).

Claims are directed to a method for preparing a nerve tissue for use as a nerve graft wherein method comprises 1) step of culturing the nerve tissue in vitro and 2) step of killing the nerve tissue. Some claims are further drawn to culture conditions including time 24-96 hours, temperature 10°C to 37°C and DMEM medium. Some claims are further drawn to the nerve tissues being mammalian or rodent tissues. Some claims are further drawn to killing by chemical treatment. Some claims are further drawn to adding a generic adhesive to the nerve tissue.

The reference by La Fleur et al. discloses a method for treating mammalian nerve tissue wherein method comprises 1) step of "culturing" the nerve tissue in vitro in DMEM medium comprising various supplements at temperature 37°C for various periods of time including 12, 24 and 2) step of "killing" the nerve tissue by chemical treatment for further extraction of proteins, RNA and other components (page 2312, column 2, par. 1-2). The nerve tissues or nerve segments are held or adhered to plastic dishes and, thus, combined with a generic adhesive. The nerve tissues derived from sciatic nerves that connected to both central and peripheral nervous system tissues.

The cited reference comprises identical active steps of culturing and killing nerve tissues under conditions as presently claimed. Thus, the cited reference anticipates the claimed invention.

2. Claims 1-4, 6-15, 17-23, 30-40, 42-56 and 116-123 are rejected under 35 U.S.C. 102(b) as being anticipated by Lassner et al. (IDS reference; J. Reconstruct. Microsurg. 1995, 11 (6): 447-453).

Claims are directed to a method for preparing a nerve tissue for use as a nerve graft wherein method comprises 1) step of culturing the nerve tissue in vitro and 2) step of killing the

nerve tissue. Some claims are further drawn to culture conditions including time 24-96 hours, temperature 10°C to 37°C and DMEM medium. Some claims are further drawn to the nerve tissues being mammalian or rodent tissues. Some claims are further drawn to killing by freezing. Some claims are further drawn to adding a generic adhesive to the nerve tissue.

The reference by Lassner et al. discloses a method for preparing a nerve tissue for use as a nerve graft wherein method comprises 1) step of culturing the nerve tissue segments in vitro under culture conditions including temperature permissive for cellular outgrowth or 37°C, time 48 hours and DMEM medium with serum, and 2) step of killing the nerve tissue by freezing at -18°C; fro example: see page 448, column 2, last paragraph relating to second series of experiments. The nerve tissues or nerve segments are held or adhered to plastic dishes and, thus, combined with a generic adhesive. The nerve tissues derived from sciatic nerves that connected to both central and peripheral nervous system tissues.

The cited reference comprises identical active steps of culturing and killing nerve tissues under conditions as presently claimed. Thus, the cited reference anticipates the claimed invention.

3. Claims 1-4, 6-15, 17-21, 30-32, 34-40, 42-45, 47-51, 53-56, 116-, 119, 122, 123 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,448,076 (Dennis et al).

Claims are directed to a method for preparing a nerve tissue for use as a nerve graft wherein method comprises 1) step of culturing the nerve tissue in vitro and 2) step of killing the nerve tissue. Some claims are further drawn to culture conditions including time 24-96 hours, temperature 10°C to 37°C and a medium. Some claims are further drawn to the nerve tissues

being mammalian or rodent tissues. Some claims are further drawn to killing by chemical treatment. Some claims are further drawn to adding a generic adhesive to the nerve tissue.

US 6,448,076 discloses a method for preparing a nerve tissue for use as a nerve graft (entire document including abstract) wherein the method comprises step of culturing *in vitro* the nerve graft in a medium or in a balanced salt solution (col. 3, lines 45-46), step of rendering the nerve graft acellular by chemical treatment (col. 3, lines 47-67 and col. 4, lines 26). The nerve graft is a mammalian peripheral nerve segment (col. 3, line 42). The cited patent discloses the 24-96 hours as time intervals for culturing or treating steps and the same temperature ranges including room temperature as required by the presently claimed method. Thus, the cited patent US 6,448,076 appears to teach the same active steps and the same structural elements as claimed. The cited patent US 6,448,076 teaches that the treated nerve graft supported axonal regeneration (col. 6, line 21-24) and, therefore, the nerve graft in the cited method was cultured under "predegenerating conditions that remodel the nerve graft and that increase neurite-promoting activity of the nerve graft upon implantation" within the meaning of the instant claims or under conditions "permissive to the activation" of cells or enzymes of the nerve graft within the meaning of the instant claims.

Therefore, US 6,448,076 anticipates the presently claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-23, 30-40, 42-56 and 116-123 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,448,076 (Dennis et al), La Fleur et al. (IDS reference; J. Exp. Med. 1996, 184:2311-2326), Ide et al. (IDS reference; "Schwann cell basal lamina and nerve regeneration". Brain Research. 1983, 288:61-75) and Evans et al. (IDS reference; Progress in Neurobiology, 1994. Vol. 43, pages 187-233).

Claims are directed to a method for preparing a nerve tissue for use as a nerve graft wherein method comprises 1) step of culturing the nerve tissue in vitro and 2) step of killing the nerve tissue. Some claims are further drawn to culture conditions including time 24-96 hours, temperature 10°C to 37°C and a medium. Some claims are further drawn to the nerve tissues being mammalian including rodent and human. Some claims are further drawn to step of killing by freezing or by chemical treatment. Some claims are further drawn to adding a generic adhesive to the nerve tissue.

US 6,448,076 (Dennis et al) is relied upon for disclosure of a method for preparing a nerve tissue for use as a nerve graft (entire document including abstract) wherein the method comprises step of culturing *in vitro* the nerve graft and step of rendering the nerve graft acellular by killing.

In particular, the cited patent US 6,448,076 (Dennis et al) discloses a chemical treatment for making acellular nerve grafts and lacks explicit teaching about rendering nerve graft acellular through killing by freezing. However, Evans et al. teaches freezing and thawing of nerve grafts for making the nerve grafts acellular and non-immunogenic (page 212. col. 2, last par.). The cited reference by Ide et al teaches that basal laminae of Schwann cells rather than living cells

play important role in nerve regeneration after implantation of nerve graft (page 62, col. 1, par. 1).

The cited patent US 6,448,076 (Dennis et al) teaches the use of balanced salt solution for graft pre-treatment before acellularization and lacks explicit teaching about the use of enriched culture media. However, La Fleur reference teaches that incubation of nerve segments in culture medium supplemented with cytokines results in up regulation of TIMP-1 expression and that TIMP-1 protects basement membrane of nerve tissue from uncontrolled degradation after injury (abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute a supplemented culture medium for a buffered salt solution in two-step method of US 6,448,076 (Dennis et al) with a reasonable expectation in success in making nerve tissues as intended for nerve grafts because culturing nerve tissues promotes up-regulation of compounds that protect basement membrane of nerve tissues from uncontrolled degradation after injury as adequately taught by La Fleur et al.

One of skill in the art would have been motivated to kill nerve graft living tissues in order to avoid tissue rejection upon transplantation as clearly taught by Evans et al. Killing by chemical treatment and killing by freezing are considered to be substitution of equivalents.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

February 3, 2006

VERA AFREMOVA

PRIMARY EXAMINER